

Letter to the Editor: New Observation

Paraneoplastic Opsoclonus-Myoclonus Syndrome Associated with Non-Small Cell Lung Cancer

David Bayless¹ , Christopher Itoh² and Rafid Mustafa² 

¹Department of Internal Medicine, Mayo Clinic, Rochester, MN, USA and ²Department of Neurology, Mayo Clinic, Rochester, MN, USA

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Opsoclonus-myoclonus syndrome (OMS; also known as opsoclonus-myoclonus-ataxia or “dancing eyes-dancing feet” syndrome) is a rare, often paraneoplastic neurological disorder, whose hallmark symptoms are opsoclonus, myoclonus, ataxia, and encephalopathy.¹ Opsoclonus is a striking oculomotor phenomenon characterized by chaotic ocular saccadic movements that occur synchronously in multiple directions and are involuntary.¹ Here, we present a case of OMS that occurred in association with non-small cell lung cancer (NSCLC).

The patient is a 73-year-old woman who initially presented with dizziness and diplopia, which began during the week prior to presentation. She had a past medical history of mild expressive aphasia secondary to a previous left basal ganglia infarct, hypertension, hyperlipidemia, and type 2 diabetes mellitus. She also had a 60-pack-year history of smoking. Neurological exam showed opsoclonus (Video, Figure 1 Panel A) and a faint, fine postural tremor of the left hand. No myoclonus or ataxia was appreciated at the time. Renal, liver, and thyroid function tests were unremarkable. An MRI of the brain with and without contrast was obtained and revealed bilateral temporal lobe T2 hyperintensity (Figure 1 Panel B), concerning encephalitis. CSF studies revealed 32 nucleated cells/ μ L (reference value, $<= 5$), a protein level of 48 mg/dL (reference value, $<= 35$), and a normal glucose. Infectious studies were negative and included blood cultures, serum HIV screen, and CSF testing for HSV 1/2, VZV, EBV, Enterovirus, *Tropheryma whipplei*, West Nile virus, and Powassan virus. CSF and serum autoimmune and paraneoplastic antibody panels were negative. FDG-PET of the body demonstrated a large right lung mass (Figure 1 Panel C), with biopsy revealing poorly differentiated NSCLC. The patient was treated with glucocorticoids (1 g of IV methylprednisolone daily for 5 days) and plasmapheresis (5 sessions) for paraneoplastic encephalitis, as well as with concurrent chemotherapy. Despite these treatments, her condition unfortunately worsened, with development of visual agnosia, expressive aphasia, autonomic dysfunction, and bilateral arm myoclonus. She was later discharged home on hospice care and passed away soon after this.

Given the patient’s opsoclonus and later development of myoclonus and encephalopathy in the setting of newly diagnosed NSCLC, with negative infectious studies and other workups, the most likely diagnosis, in this case, is paraneoplastic OMS (P-OMS).

The diagnosis is further supported by the rapid progression of the patient’s symptoms, which is characteristic of P-OMS.² The patient did have negative autoantibody testing results, but this is a common finding in P-OMS. In one retrospective cohort study of 114 patients with OMS, 45 of whom had P-OMS, autoantibodies were found in only 11% of patients.³ Autoantibodies identified in patients with P-OMS and lung cancer in this study included those against the glycine receptor, Ma2, Zic4, and HNK-1.³

The pathogenesis of P-OMS is incompletely understood but is thought to have an autoimmune basis, possibly with both humoral and cell-mediated immunologic mechanisms.⁴ What drives the opsoclonus itself is also unclear, though the three leading hypotheses implicate pathologic changes to the cerebellum or brainstem.⁴ The first hypothesis posits damage of the omnipause neurons of the pons as the cause of opsoclonus; the second (the “brainstem theory”) proposes that changes in the activity of saccadic burst neurons of the brainstem constitute the mechanistic basis; the third (the “cerebellar theory”) states that disinhibition of the fastigial nuclei of the cerebellum is to blame.⁴ Among these, the latter two hypotheses appear to have more evidence in their favor than the first one.⁴

If OMS is identified, an underlying etiology should be sought, particularly because this can influence treatment and prognosis of the OMS.^{2,5} Malignancy is the most frequently identified cause of OMS, and evaluation for occult malignancy is an important part of the diagnostic workup in all patients with OMS.¹ Neuroblastoma is the malignancy most commonly associated with P-OMS in children, whereas in adults, it is small-cell lung cancer.^{1,3} Our case is unusual in that there are only a limited number of other cases in the literature that report P-OMS occurring in association with NSCLC.^{2,6–8} We are not aware of any other cases of P-OMS secondary to NSCLC in which plasmapheresis was utilized for management.

Other etiologies of OMS to consider include infections such as HIV, Lyme disease, and West Nile virus; multiple sclerosis; systemic diseases such as celiac disease and sarcoidosis; metabolic derangements such as hyperosmolar coma; and medications such as lithium.¹ It is worth noting that in many instances, no etiology of the OMS is ever identified.^{1,5}

Treatment of P-OMS is directed at the underlying malignancy as well as the autoimmune mechanisms thought to be responsible for

Corresponding author: R. Mustafa; Email: mustafa.rafid@mayo.edu

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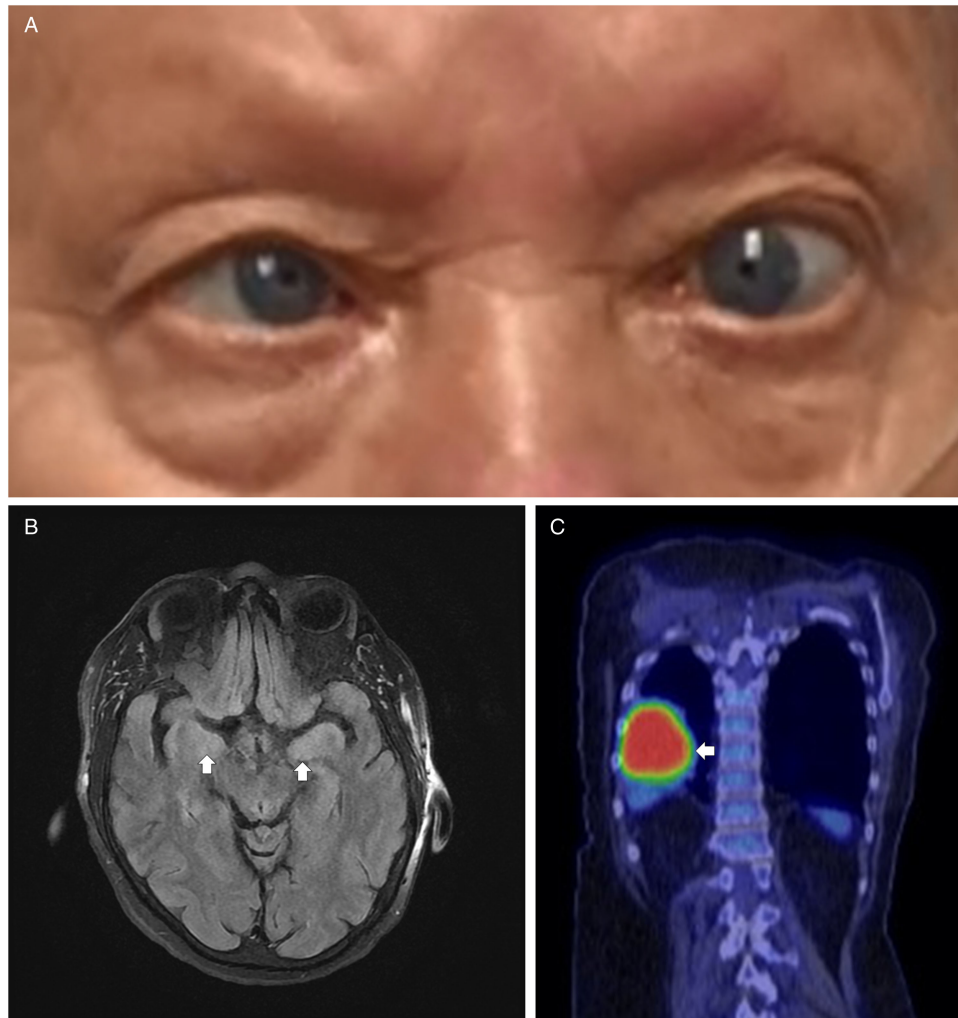


Figure 1: Clinical findings in a 73-year-old woman with paraneoplastic opsoclonus-myoclonus syndrome. **a.** Still image of opsoclonus footage showing dysconjugate gaze. **b.** MRI brain T2-weighted sequence showing bilateral temporal lobe hyperintensity (arrows), suggestive of encephalitis. **c.** FDG-PET imaging demonstrating a large right lung mass (arrow), later diagnosed as poorly differentiated non-small cell lung cancer.

the disorder. Chemotherapy for the malignancy can be beneficial not only for its antineoplastic effect but also because of induced immunosuppression.⁵ Apart from chemotherapy, immunomodulatory medications that have been used with success in OMS include glucocorticoids, rituximab, and intravenous immunoglobulin (IVIG).⁴ Plasmapheresis can be considered for patients who are refractory to IVIG or glucocorticoid monotherapy (as was the case with our patient).⁴ Even with appropriate treatment, the prognosis of P-OMS is often poor.²

Our case illustrates how the isolated neurological finding of opsoclonus can aid in the discovery of a serious underlying condition, and it showcases that OMS can occur even with malignancies, such as NSCLC, which are not commonly associated with OMS. It also illustrates that myoclonus may not manifest until days after the onset of opsoclonus. Finally, our patient's clinical deterioration over the course of just weeks, considered alongside data showing poor outcomes in a significant proportion of those with P-OMS, suggests that progression of neurological symptoms while on active cancer treatment and immunosuppression should prompt consideration of goals of care discussion or, if appropriate, escalation of therapy.²

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/cjn.2023.329>.

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Dr Bayless: writing – original draft, writing – review and editing, investigation.

Dr Itoh: conceptualization, writing – review and editing.

Dr Mustafa: writing – original draft, writing – review and editing, supervision.

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